[Committee Print]

110TH CONGRESS
1ST SESSION

H. R. _____

To amend the Federal Food, Drug, and Cosmetic Act to improve drug safety, and for other purposes.

IN THE HOUSE OF REPRESENTATIVES

M__. _____ introduced the following bill; which was referred to the Committee on _____

A BILL

To amend the Federal Food, Drug, and Cosmetic Act to improve drug safety, and for other purposes.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. RISK EVALUATION AND MITIGATION STRATEGIES FOR HUMAN DRUGS.

(a) IN GENERAL.—Section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) is amended by adding at the end the following:

''(o) RELATION TO SECTION 301.—

''(1) IN GENERAL.—A person may not introduce or deliver for introduction into interstate commerce a new drug unless, subject to section 505A(a)(4)—

''(A) the application approved under subsection (b) or (j), or under section 351 of the Public Health Service Act, as applicable, contains a risk evaluation and mitigation strategy approved under section 505A; and

''(B) the person is in compliance with the requirements of the strategy and with other requirements under section 505A, including requirements regarding assessments of approved strategies.

''(2) CERTAIN POSTMARKET STUDIES.—The failure to conduct a postmarket study under subpart H of part 314 of title 21, Code of Federal Regulations (or any successor regulation), is deemed to be a violation of paragraph (1).''.

(b) REQUIREMENTS REGARDING STRATEGIES.—Chapter V of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 351 et seq.) is amended—

(1) by redesignating section 505A as 505A–1; and

(2) by inserting after section 505 the following section:

"SEC. 505A. RISK EVALUATION AND MITIGATION STRATEGIES.

''(a) SUBMISSION OF PROPOSED STRATEGY.—

''(1) INITIAL APPROVAL.—A person who submits an application referred to in section 505(o)(1) (referred to in this section as an 'applicant') shall include in the application a proposed risk evaluation and mitigation strategy, subject to paragraph (4).

''(2) APPROVAL OF NEW INDICATION FOR USE.—In the case of a drug for which an approved application under section 505(b) or under section 351 of the Public Health Service Act was in effect on the day before the effective date of this section, if the drug is subject to section 503(b) the applicant shall include a proposed risk evaluation and mitigation strategy in any application submitted to the Secretary seeking approval of a new indication for use of the drug.

''(3) ABBREVIATED NEW DRUG APPLICATIONS.—The applicability of this section to an application under section 505(j) is subject to subsection (i).

''(4) WAIVERS.—

''(A) IN GENERAL.—The Secretary may waive the applicability of paragraph (1) to an application if the Secretary determines that there is substantial evidence that the waiver will not pose a risk to any segment of the population of individuals for which the drug involved is approved.

''(B) REVOCATION OF WAIVER.—

''(i) IN GENERAL.—The Secretary may revoke a waiver under subparagraph (A) if the Secretary determines that the factual assumptions upon which the decision to grant the waiver was based have ceased to be accurate.

''(ii) PROCEDURES.—In the case of an application for which a waiver under subparagraph (A) is revoked, the Secretary shall apply paragraph (1) by requiring the holder of the approved application to submit to the Secretary a proposed risk evaluation and mitigation strategy not later than 180 days after the date on which the Secretary notifies the holder of the revocation. Pending the submission and approval of the strategy, the Secretary may apply

such elements under subsections (d), (e), (f) with respect to the drug involved as the Secretary determines to be appropriate to protect the public health.

''(C) REGULATIONS.—The Secretary shall by regulation establish conditions and procedures for granting waivers under subparagraph (A) and for revoking the waivers under subparagraph (B).

''(D) REPORTS.—Beginning one year after the effective date of this section, the Secretary shall annually submit to the Congress a report that contains—

''(i) a list of the drugs for which waivers under subparagraph (A) have been granted and a summary of the reasons underlying the decision to grant the waivers; and

''(ii) a list of the drugs for which waivers have been revoked under subparagraph (B) and a summary of the reasons underlying the decision to revoke the waivers.

''(b) DEFINITIONS.—For purposes of this section:

''(1) ADVERSE DRUG EXPERIENCE.—The term 'adverse drug experience' means any adverse event associated with the use of a drug in humans, whether or not considered drug related, including—

''(A) an adverse event occurring in the course of the use of the drug in professional practice;

''(B) an adverse event occurring from an overdose of the drug, whether accidental or intentional;

''(C) an adverse event occurring from abuse of the drug;

''(D) an adverse event occurring from withdrawal of the drug; and

''(E) any failure of expected pharmacological action of the drug.

''(2) SERIOUS ADVERSE DRUG EXPERIENCE.—The term 'serious adverse drug experience' is an adverse event that—

''(A) results in—

''(I) death;

''(ii) an adverse drug experience that places the patient at immediate risk of death from the adverse drug experience as it occurred (not including an adverse drug

experience that might have caused death had it occurred in a more severe form);

''(iii) inpatient hospitalization or prolongation of existing hospitalization;

''(iv) a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions; or

''(v) a congenital anomaly or birth defect; or

''(B) based on appropriate medical judgment, may jeopardize the patient and may require a medical or surgical intervention to prevent an outcome described under subparagraph (A).

''(3) SERIOUS RISK.—The term 'serious risk' means a risk of a serious adverse drug experience.

''(4) UNEXPECTED SERIOUS RISK.—The term 'unexpected serious risk' means a serious adverse drug experience that is not listed in the labeling of a drug, or that may be symptomatically and pathophysiologically related to an adverse drug experience identified in the labeling, but differs from such adverse drug experience because of greater severity, specificity, or prevalence.

''(5) SIGNAL OF A SERIOUS RISK.—The term 'signal of a serious risk' means information related to a serious adverse drug experience associated with use of a drug and derived from—

''(A) a clinical trial;

''(B) adverse event reports;

''(C) a postapproval study, including a study under subsection (e)(4); or

''(D) peer-reviewed biomedical literature.

''(6) NEW SAFETY INFORMATION.—The term 'new safety information' with respect to a drug means information about—

''(A) a serious risk or an unexpected serious risk associated with use of the drug that the Secretary has become aware of since the last assessment of the approved risk evaluation and mitigation strategy for the drug; or

''(B) the effectiveness of the approved risk evaluation and mitigation strategy for the drug obtained since the last assessment of such strategy.

''(c) CONTENTS.—A proposed risk evaluation and mitigation strategy under subsection (a) shall—

''(1) include the elements required under subsection (d); and

''(2) to the extent required by the Secretary, include additional elements described in subsections (e) and (f).

''(d) MINIMAL REQUIRED ELEMENTS OF STRATEGY.—For purposes of subsection (C)(1), the risk evaluation and mitigation strategy for a drug shall require the following:

''(1) With respect to labeling:

''(A) Labeling for use by health care providers as approved under section 505(c)).

''(B) For the first 2 years (or for such period as the Secretary determines on a case-by-case basis to be appropriate) after the drug or a new indication for the drug is approved, inclusion in the labeling and any direct-to-consumer advertisements of a unique symbol indicating the newly approved status of the drug or indication.

''(2) With respect to reports:

''(A) Submission of reports for the drug as required under section 505(k).

''(B) For a drug that is a vaccine—

''(I) an analysis of reports to the Vaccine Adverse Event Reporting Systems (VAERS); or

"(ii) surveillance using the Vaccine Safety Datalink (VSD) or successor databases.

"(3) A pharmacovigilance statement—

"(A) as to whether the reports under paragraph (2)(A) or, for a vaccine, the analysis and surveillance under paragraph (2)(B), and the periodic assessment under paragraph (5), are sufficient to assess the serious risks and to identify unexpected serious risks of the drug; and

"(B) if such reports, such analysis and surveillance, and such periodic assessment are not sufficient to assess the serious risks and to identify unexpected serious risks of the drug, that describes what study or studies of the drug are required under subsection (d)(4) or what clinical trial or trials of the drug are required under subsection (d)(5).

"(4) A justification for the pharmacovigilance statement in paragraph (3) that takes into consideration—

"(A) the estimated size of the treatment population for the drug;

"(B) the seriousness of the disease or condition that the drug is used to treat or prevent;

"(C) the expected or actual duration of treatment with the drug;

"(D) the availability and safety of a drug or other treatment, if any, for such disease or condition to which the safety of the drug may be compared; and

"(E) the seriousness of the risk at issue and its background incidence in the population.

"(5) A timetable for submission of assessments of the strategy that—

"(A) is not less frequent than once annually for the first 3 years after the drug is initially approved under section 505 or licensed under section 351 of the Public Health Service Act;

"(B) includes an assessment in the seventh year after the drug is so approved; and

"(C) subject to subparagraph (B), for subsequent years—

"(I) is at a frequency specified in the strategy;

''(ii) is increased or reduced in frequency as necessary as provided for in subsection (g)(4)(F); and

''(iii) is eliminated after the 3-year period described in subparagraph (A) if the Secretary determines that serious risks of the drug have been adequately identified and assessed and are being adequately managed.

''(e) ADDITIONAL POTENTIAL ELEMENTS OF STRATEGY.—

''(1) IN GENERAL.—The Secretary may under subsection (c)(2) require that the risk evaluation and mitigation strategy for a drug include 1 or more of the additional elements described in this subsection if the Secretary makes the determination required with respect to each additional included element.

''(2) MEDGUIDE; PATIENT PACKAGE INSERT.—The risk evaluation and mitigation strategy for a drug may require that the applicant develop for distribution to each patient when the drug is dispensed—

"(A) a Medication Guide, as provided for under part 208 of title 21, Code of Federal Regulations (or any successor regulations); and

"(B) a patient package insert, if the Secretary determines that such insert may help mitigate a serious risk of the drug.

"(3) COMMUNICATION PLAN.—The risk evaluation and mitigation strategy for a drug may require that the applicant conduct a communication plan to health care providers, if, with respect to such drug, the Secretary determines that such plan may support implementation of an element of the strategy. Such plan may include—

"(A) sending letters to health care providers;

"(B) disseminating information about the elements of the risk evaluation and mitigation strategy to encourage implementation by health care providers of components that apply to such health care providers, or to explain certain safety protocols (such as medical monitoring by periodic laboratory tests); or

"(C) disseminating information to health care providers through professional societies

about any serious risks of the drug and any protocol to assure safe use.

''(4) POSTAPPROVAL STUDIES.—The risk evaluation and mitigation strategy for a drug may require that the applicant conduct, or provide that the Secretary will conduct, an appropriate postapproval study, such as a prospective or retrospective observational study (including through the systematic use of established health care networks and databases), of the drug (with a target schedule for completing the study and reporting the results to the Secretary), if the Secretary determines the reports, analysis and surveillance, and periodic assessments referred to in subsection (d)(3) are not sufficient to—

''(A) assess evidence of a serious risk related to the safety or effectiveness of the drug; or

''(B) identify unexpected serious risks in domestic populations who use the drug, including populations not included in studies used to approve the drug (such as older people, people with comorbidities, pregnant women, or children).

''(5) POSTAPPROVAL CLINICAL TRIALS.—

''(A) IN GENERAL.—The risk evaluation and mitigation strategy for a drug may require that the applicant for a drug for which there is no effective approved application under section 505(j) as of the date that the requirement is first imposed conduct an appropriate post-approval clinical trial of the drug (with a target schedule for completing the clinical trial and reporting the results to the Secretary) to be included in the clinical trial registry database and clinical trial results database provided for under section 402(I) of the Public Health Service Act, if the Secretary determines that a study or studies under paragraph (4) will likely be inadequate to assess evidence of a serious risk related to the safety or effectiveness of the drug.

''(B) RULE OF CONSTRUCTION.—Subparagraph (A) may not be construed as having any affect on the authority of the Secretary under section 506 or under subpart H of part 314 of title 21, Code of Federal Regulations (or any successor regulation).

''(6) PRECLEARANCE.—

''(A) IN GENERAL.—The risk evaluation and mitigation strategy for a drug may require

that the applicant submit to the Secretary advertisements of the drug for preclearance, if the Secretary determines that such preclearance is necessary to ensure compliance with section 502(n) with respect to the disclosure of information about a serious risk listed in the labeling of the drug. The advertisements required to be submitted under the preceding sentence shall be reviewed and cleared by the Secretary within 45 days of submission.

''(B) SPECIFICATION OF ADVERTISEMENTS.—The Secretary may specify the advertisements required to be submitted under subparagraph (A).

''(7) SPECIFIC DISCLOSURES.—

''(A) IN GENERAL.—The risk evaluation and mitigation strategy for a drug may require that the applicant include in advertisements of the drug a specific disclosure—

''(I) of the date the drug was approved and that the existing information may not have identified or allowed for full assessment of all serious risks of using the drug, if the Secretary determines that such

disclosure is necessary to protect public health and safety; or

''(ii) about a serious adverse event listed in the labeling of the drug or a protocol to ensure safe use described in the labeling of the drug, if the Secretary determines that such advertisements lacking such disclosure would be false or misleading.

''(B) SPECIFICATION OF ADVERTISEMENTS.—The Secretary may specify the advertisements required to include a specific disclosure under subparagraph (A).

''(8) TEMPORARY REVIEW PERIOD.—The risk evaluation and mitigation strategy for a drug may require that for a fixed period after initial approval, not to exceed 3 years, the applicant not issue or cause to be issued direct-to-consumer advertisements of the drug, if the Secretary determines that disclosure under paragraph (7) is inadequate to protect public health and safety, and that such prohibition is necessary to protect public health and safety while additional information about serious risks of the drug is collected, considering—

"(A) the number of patients who may be treated with the drug;

"(B) the seriousness of the condition for which the drug will be used;

"(C) the serious adverse events listed in the labeling of the drug;

"(D) the extent to which patients have access to other approved drugs in the pharmacological class of the drug and with the same intended use as the drug; and

"(E) the extent to which clinical trials used to approve the drug may not have identified serious risks that might occur among patients expected to be treated with the drug.

"(f) RESTRICTIONS ON DISTRIBUTION OR USE.—

"(1) IN GENERAL.—If the Secretary determines that a drug shown to be effective can be safely used only if distribution or use of such drug is restricted, the Secretary may under subsection (c)(2) require as elements of the risk evaluation and mitigation strategy such restrictions on distribution or use as are needed to ensure safe use of the drug.

"(2) LIMITS ON RESTRICTIONS.—Restrictions under paragraph (1) regarding a drug shall—

''(A) be commensurate with the specific risk presented by the drug;

''(B) not be unduly burdensome on patient access to the drug, particularly for patients with serious or life-threatening diseases or conditions; and

''(C) to the extent practicable, conform with restrictions on distribution or use for other drugs with similar risks, so as to minimize the burden on the health care delivery system.

''(3) ELEMENTS.—The restrictions on distribution or use described in paragraph (1) shall include 1 or more goals to evaluate or mitigate a serious risk listed in the labeling of the drug, and may require that—

''(A) health care providers that prescribe the drug have special training or experience, or are specially certified;

''(B) pharmacies, practitioners, or health care settings that dispense the drug are specially certified;

''(C) the drug be dispensed to patients only in certain health care settings, such as hospitals;

''(D) the drug be dispensed to patients with evidence or other documentation of safe-use conditions, such as laboratory test results;

''(E) each patient using the drug be subject to certain monitoring; or

''(F) each patient using the drug be enrolled in a registry.

''(4) IMPLEMENTATION SYSTEM.—The restrictions on distribution or use described in paragraph (1) may require a system through which the applicant is able to—

''(A) monitor and evaluate implementation of the restrictions by health care providers, pharmacists, patients, and other parties in the health care system who are responsible for implementing the restrictions;

''(B) work to improve implementation of the restrictions by health care providers, pharmacists, patients, and other parties in the health care system who are responsible for implementing the restrictions; and

''(C) stop distribution of the drug to those health care providers, pharmacists, and other parties in the health care system—

"(I) who are responsible for implementing the restrictions; and

"(ii) whom the applicant knows have failed to meet their responsibilities for implementing the restrictions, after the applicant has informed such party of such failure and such party has not remedied such failure.

"(5) PATENTS.—The Secretary shall not approve a risk evaluation and mitigation strategy for a drug, or any modification to the strategy, under subsection (a) if—

"(A) the strategy includes a restriction on distribution or use described in paragraph (1) that is protected by a patent;

"(B) such patent was issued after the date of the enactment of this section; and

"(C) such patent would prohibit or impair the application of such restriction under subsection (I)(1)(G) to a drug that is the subject of an abbreviated new drug application.

"(g) ASSESSMENT AND MODIFICATION OF APPROVED STRATEGY.—

"(1) VOLUNTARY ASSESSMENTS.—A person who is the holder of an approved application that

contains an approved risk evaluation and mitigation strategy under subsection (a) (referred to in this subsection as the 'responsible person') may, subject to paragraph (2), submit to the Secretary an assessment of, and propose a modification to, the approved strategy for the drug involved at any time.

''(2) REQUIRED ASSESSMENTS.—A responsible person shall, subject to paragraph (5), submit an assessment of, and may propose a modification to, the approved risk evaluation and mitigation strategy for a drug—

''(A) when submitting a supplemental application for a new indication for use under section 505(b) or under section 351 of the Public Health Service Act, unless the drug is not subject to section 503(b) and the risk evaluation and mitigation strategy for the drug includes only the elements under subsection (d);

''(B) when required by the strategy, as provided for in the timetable under subsection (d)(5);

''(C) within a time specified by the Secretary, not to be less than 45 days, when ordered by the Secretary, if the Secretary determines that new safety or effectiveness informa-

tion indicates that an element under subsection (d) or (e) should be modified or included in the strategy;

''(D) within 90 days when ordered by the Secretary, if the Secretary determines that new safety or effectiveness information indicates that an element under subsection (f)should be modified or included in the strategy; or

''(E) within 15 days when ordered by the Secretary, if the Secretary determines that there may be a cause for action by the Secretary under section 505(e).

''(3) REQUIREMENTS FOR ASSESSMENTS.—An assessment under paragraph (1) or (2) of an approved risk evaluation and mitigation strategy for a drug shall include—

''(A) with respect to any goal under subsection (f), an assessment of the extent to which the restrictions on distribution or use are meeting the goal or whether the goal or such restrictions should be modified;

''(B) with respect to any postapproval study required under subsection (e)(4), the status of such study, including whether any dif-

ficulties completing the study have been encountered; and

''(C) with respect to any postapproval clinical trial required under subsection (e)(5), the status of such clinical trial, including whether enrollment has begun, the number of participants enrolled, the expected completion date, whether any difficulties completing the clinical trial have been encountered, and registration information with respect to requirements under section 402(I) of the Public Health Service Act.

''(4) MODIFICATION.—A modification (whether an enhancement or a reduction) to the approved risk evaluation and mitigation strategy for a drug may include the addition or modification of any element under paragraph (1), (2), or (3) of subsection (d) or the addition, modification, or removal of any element under subsection (e) or (f), such as—

''(A) a labeling change, including the addition of a boxed warning;

''(B) adding a postapproval study or clinical trial requirement;

''(C) modifying a postapproval study or clinical trial requirement (such as a change in

trial design due to legitimate difficulties recruiting participants);

"(D) adding, modifying, or removing a restriction on advertising under paragraph (6), (7), or (8) of subsection (e);

"(E) adding, modifying, or removing a restriction on distribution or use under subsection (f); or

"(F) modifying the timetable for assessments of the strategy under subsection (d)(5), including to eliminate assessments.

"(5) NO EFFECT ON LABELING CHANGES THAT DO NOT REQUIRE PREAPPROVAL.—In the case of a labeling change to which section 314.70 of title 21, Code of Federal Regulations (or any successor regulation), applies for which the submission of a supplemental application is not required or for which distribution of the drug involved may commence upon the receipt by the Secretary of a supplemental application for the change, the submission of an assessment of the approved risk evaluation and mitigation strategy for the drug under paragraph (2) is not required.

"(h) REVIEW OF PROPOSED STRATEGIES; REVIEW OF ASSESSMENTS OF APPROVED STRATEGIES.—

''(1) IN GENERAL.—The Secretary shall promptly review each proposed risk evaluation and mitigation strategy for a drug submitted under subsection (a) and each assessment of an approved risk evaluation and mitigation strategy for a drug submitted under subsection (g).

''(2) MARKETING PLAN.—As part of a review conducted under this subsection, the Secretary may require the applicant or responsible person involved (referred to in this subsection as the 'reviewed entity') to submit the marketing plan of the reviewed entity for the drug in order to allow the Secretary to determine whether any of the proposed or ongoing marketing activities undermine any of the requirements of the risk evaluation and mitigation strategy.

''(3) DISCUSSION.—The Secretary shall initiate discussions with a reviewed entity for purposes of this subsection to determine a strategy—

''(A) if the proposed strategy or assessment is submitted as part of an application or supplemental application under subsection (a) or subsection (g)(1)(A), not less than 60 days before the action deadline for the application that has been agreed to by the Secretary and that has been set forth in goals identified in let-

ters of the Secretary (relating to the use of fees collected under section 736 to expedite the drug development process and the process for the review of human drug applications);

''(B) if the assessment is submitted under subparagraph (B) or (C)) or subsection (g)(2), not later than 20 days after such submission;

''(C) if the assessment is submitted under subsection (g)(1) or subsection (g)(2)(D) , not later than 30 days after such submission; or

''(D) if the assessment is submitted under subsection (g)(2)(E), not later than 10 days after such submission.

''(4) ACTION.—

''(A) IN GENERAL.—Unless the reviewed entity requests the dispute resolution process described under paragraph (5), the Secretary shall approve and describe the risk evaluation and mitigation strategy for a drug, or any modification to the strategy—

''(I) as part of the action letter on the application, when a proposed strategy is submitted under subsection (a) or an assessment of the strategy is submitted under subsection (g)(1)(A); or

''(ii) in an order issued not later than 50 days after the date discussions of such modification begin under paragraph (3), when an assessment of the strategy is submitted under subsection (g)(1) or under any of subparagraphs (B) through (E) of subsection (g)(2).

''(B) INACTION.—An approved risk evaluation and mitigation strategy shall remain in effect until the Secretary acts, if the Secretary fails to act as provided under subparagraph (A).

''(C) PUBLIC AVAILABILITY.—Any action letter described in subparagraph (A)(I) or order described in subparagraph (A)(ii) shall be made publicly available.

''(5) DISPUTE RESOLUTION.—

''(A) REQUEST FOR REVIEW.—Not earlier than 15 days, and not later than 35 days, after discussions under paragraph (3) have begun, the reviewed entity may request in writing that a dispute about the strategy be reviewed by the Drug Safety Oversight Board under subsection (j). Upon receipt of such a request, the Secretary shall schedule the dispute for review

under subparagraph (B) and, not later than 5 business days of scheduling the dispute for review, shall publish by posting on the Internet or otherwise a notice that the dispute will be reviewed by the Drug Safety Oversight Board.

''(B) SCHEDULING REVIEW.—If a reviewed entity requests review under subparagraph (A), the Secretary—

''(I) shall schedule the dispute for review at 1 of the next 2 regular meetings of the Drug Safety Oversight Board, whichever meeting date is more practicable; or

''(ii) may convene a special meeting of the Drug Safety Oversight Board to review the matter more promptly, including to meet an action deadline on an application (including a supplemental application).

''(C) AGREEMENT AFTER DISCUSSION OR ADMINISTRATIVE APPEALS.—

''(I) FURTHER DISCUSSION OR ADMINISTRATIVE APPEALS.—A request for review under subparagraph (A) shall not preclude further discussions to reach agreement on the risk evaluation and mitigation strategy, and such a request shall

not preclude the use of administrative appeals within the Food and Drug Administration to reach agreement on the strategy, including appeals as described in letters of the Secretary (relating to the use of fees collected under section 736 to expedite the drug development process and the process for the review of human drug applications) for procedural or scientific matters involving the review of human drug applications and supplemental applications that cannot be resolved at the divisional level.

''(ii) AGREEMENT TERMINATES DISPUTE RESOLUTION.—At any time before a decision and order is issued under subparagraph (G) , the Secretary and the reviewed entity may reach an agreement on the risk evaluation and mitigation strategy through further discussion or administrative appeals, terminating the dispute resolution process, and the Secretary shall issue an action letter or order, as appropriate, that describes the strategy.

''(D) MEETING OF THE BOARD.—At a meeting of the Drug Safety Oversight Board

described in subparagraph (B), the Board shall—

"(I) hear from both parties; and

"(ii) review the dispute.

"(E) RECORD OF PROCEEDINGS.—The Secretary shall ensure that the proceedings of any such meeting are recorded, transcribed, and made public within 30 days of the meeting. The Secretary shall redact the transcript to protect any trade secrets or other confidential information described in section 552(b)(4) of title 5, United States Code.

"(F) RECOMMENDATION OF THE BOARD.—Not later than 5 days after any such meeting, the Drug Safety Oversight Board shall provide a written recommendation on resolving the dispute to the Secretary. Not later than 5 days after the Board provides such written recommendation to the Secretary, the Secretary shall make the recommendation available to the public.

"(G) ACTION BY THE SECRETARY.—

"(I) ACTION LETTER.—With respect to a proposal or assessment referred to in paragraph (1), the Secretary shall issue an

action letter that resolves the dispute not later than the later of—

''(I) the action deadline referred to in paragraph (3)(A); or

''(II) 7 days after receiving the recommendation of the Drug Safety Oversight Board.

''(ii) ORDER.—With respect to an assessment of an approved risk evaluation and mitigation strategy under subsection (g)(1) or under any of subparagraphs (B) through (E) of subsection (g)(2), the Secretary shall issue an order, which shall be made public, that resolves the dispute not later than 7 days after receiving the recommendation of the Drug Safety Oversight Board.

''(H) INACTION.—An approved risk evaluation and mitigation strategy shall remain in effect until the Secretary acts, if the Secretary fails to act as provided for under subparagraph (G).

''(I) EFFECT ON ACTION DEADLINE.—With respect to a proposal or assessment referred to in paragraph (1), the Secretary shall

be considered to have met the action deadline referred to in paragraph (3)(A) with respect to the application involved if the reviewed entity requests the dispute resolution process described in this paragraph and if the Secretary—

"(I) has initiated the discussions described under paragraph (3) not less than 60 days before such action deadline; and

"(ii) has complied with the timing requirements of scheduling review by the Drug Safety Oversight Board, providing a written recommendation, and issuing an action letter under subparagraphs (B), (F), and (G), respectively.

"(J) DISQUALIFICATION.—No individual who is an employee of the Food and Drug Administration and who reviews a drug or who participated in an administrative appeal under subparagraph (C)(I) with respect to such drug may serve on the Drug Safety Oversight Board at a meeting under subparagraph (D) to review a dispute about the risk evaluation and mitigation strategy for such drug.

"(K) ADDITIONAL EXPERTISE.—The Drug Safety Oversight Board may add members with

relevant expertise from the Food and Drug Administration, including the Office of Pediatrics, the Office of Women's Health, or the Office of Rare Diseases, or from other Federal public health or health care agencies, for a meeting under subparagraph (D) of the Drug Safety Oversight Board.

''(6) USE OF ADVISORY COMMITTEES.—The Secretary may convene a meeting of 1 or more advisory committees of the Food and Drug Administration to—

''(A) review a concern about the safety of a drug or class of drugs, including before an assessment of the risk evaluation and mitigation strategy or strategies of such drug or drugs is required to be submitted under any of subparagraphs (B) through (E) of subsection (g)(2);

''(B) review the risk evaluation and mitigation strategy or strategies of a drug or group of drugs; or

''(C) review a dispute under paragraph (5).

''(7) PROCESS FOR ADDRESSING DRUG CLASS EFFECTS.—

''(A) IN GENERAL.—When a concern about a serious risk of a drug may be related to the

pharmacological class of the drug, the Secretary may defer assessments of the approved risk evaluation and mitigation strategies for such drugs until the Secretary has convened 1 or more public meetings to consider possible responses to such concern. If the Secretary defers an assessment under this subparagraph, the Secretary shall give notice to the public of the deferral not later than 5 days of the deferral.

''(B) PUBLIC MEETINGS.—Such public meetings may include—

''(I) 1 or more meetings of the reviewed entities for such drugs;

''(ii) 1 or more meetings of 1 or more advisory committees of the Food and Drug Administration, as provided for under paragraph (6); or

''(iii) 1 or more workshops of scientific experts and other stakeholders.

''(C) ACTION.—After considering the discussions from any meetings under subparagraph (B), the Secretary may—

''(I) announce in the Federal Register a planned regulatory action, including a modification to each risk evaluation and

mitigation strategy, for drugs in the pharmacological class;

"(ii) seek public comment about such action; and

"(iii) after seeking such comment, issue an order addressing such regulatory action.

"(8) INTERNATIONAL COORDINATION.—The Secretary may coordinate the timetable for submission of assessments under subsection (d)(5), a study under subsection (e)(4), or a clinical trial under subsection (e)(5), with efforts to identify and assess the serious risks of such drug by the marketing authorities of other countries whose drug approval and risk management processes the Secretary deems comparable to the drug approval and risk management processes of the United States. If the Secretary takes action to coordinate such timetable, the Secretary shall give notice to the public of the action not later than 5 days after the action.

"(9) EFFECT.—Use of the processes described in paragraphs (7) and (8) shall not delay action on an application or a supplement to an application for a drug.

"(i) ABBREVIATED NEW DRUG APPLICATIONS.—

''(1) IN GENERAL.—A drug that is the subject of an abbreviated new drug application under section 505(j) is subject to only the following elements of the risk evaluation and mitigation strategy required under subsection (a) for the applicable listed drug:

''(A) Labeling, as required under subsection (d)(1) for the applicable listed drug.

''(B) Submission of reports, as required under subsection (d)(2)(A) for the applicable listed drug.

''(C) A Medication Guide or patient package insert, if required under subsection (e) for the applicable listed drug.

''(D) Preclearance of advertising, if required under subsection (e)(6) for the applicable listed drug.

''(E) Specific disclosures in advertising, if required under subsection (e)(7) for the applicable listed drug.

''(F) A temporary review period during which direct-to-consumer advertising will not occur, if required under subsection (e)(8) for the applicable listed drug.

''(G) Restrictions on distribution or use, if required under subsection (f) for the listed drug. A drug that is the subject of an abbreviated new drug application and the listed drug shall use a single, shared system under subsection (f)(4). The Secretary may waive the requirement under the preceding sentence for a drug that is the

subject of an abbreviated new drug application if the Secretary determines that—

''(I) it is not practical for the drug to use such single, shared system; or

''(ii) the burden of using the single, shared system outweighs the benefit of using the single system.

''(2) ACTION BY SECRETARY.—For an applicable listed drug for which a drug is approved under section 505(j), the Secretary—

''(A) shall undertake any communication plan to health care providers required under subsection (e)(3) for the applicable listed drug;

''(B) shall conduct any postapproval study required under subsection (e)(4) for the applicable listed drug; and

''(C) shall inform the applicant for the drug that is so approved if the risk evaluation and mitigation strategy for the applicable listed drug is modified.

''(j) DRUG SAFETY OVERSIGHT BOARD.—

''(1) IN GENERAL.—There is established a Drug Safety Oversight Board.

''(2) COMPOSITION; MEETINGS.—The Drug Safety Oversight Board shall—

''(A) be composed of scientists and health care practitioners appointed by the Secretary,

each of whom is an employee of the Federal Government;

''(B) include representatives from offices throughout the Food and Drug Administration;

''(C) include at least 1 representative from each of the National Institutes of Health, the Department of Health and Human Services (other than the Food and Drug Administration), and the Veterans Health Administration; and

''(D) meet at least monthly to provide oversight and advice to the Secretary on the management of important drug safety issues.''.

(c) REGULATION OF BIOLOGICAL PRODUCTS.—Section 351 of the Public Health Service Act (42 U.S.C. 262) is amended—

(1) in subsection (a)(2), by adding at the end the following:

''(D) RISK EVALUATION AND MITIGATION STRATEGY.—A person that submits an application for a license under this paragraph is subject to section 505(o) of the Federal Food, Drug, and Cosmetic Act.''; and

(2) in subsection (j), by inserting '', including the requirements under section 505(o) of such Act,'' after '', and Cosmetic Act''.

(d) CONFORMING AMENDMENT; PRECLEARANCE OF ADVERTISEMENTS.—Section 502(n)(3)(A) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 352(n)(3)(A)) is amended by inserting ''(or when required under section 505A(e)(6))'' after ''except in extraordinary circumstances''.

(e) RULE OF CONSTRUCTION REGARDING PEDIATRIC STUDIES.—This Act and the amendments made by this Act may not be construed as affecting the authority of the Secretary of Health and Human Services to request pediatric studies under section 505A–1 of the Federal Food, Drug, and Cosmetic Act or to require such studies under section 505B of such Act.

SEC. 2. ENFORCEMENT.

(a) MISBRANDING.—Section 502 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 352) is amended by adding at the end the following:

''(y) If it is a drug subject to an approved risk evaluation and mitigation strategy pursuant to section 505(o) and the person responsible for complying with the strategy fails—

''(1) to make a labeling change required by such strategy after the Secretary has completed review of, and acted on, an assessment of such strategy under section 505A(g); or

''(2) to comply with a requirement of such strategy provided for under subsection (d), (e), or (f) of section 505A.''.

(b) CIVIL PENALTIES.—Section 303 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 333(f)) is amended—

(1) by redesignating subsection (g) (relating to civil penalties) as subsection (f); and

(2) in subsection (f) (as so redesignated)—

(A) by redesignating paragraphs (3), (4), and (5) as paragraphs (4), (5), and (6), respectively;

(B) by inserting after paragraph (2) the following:

''(3) Any person who violates a requirement of this Act which relates to drugs shall be liable to the United States for a civil penalty in an amount not less than $50,000 for each such violation and, for all such violations adjudicated in a single proceeding, in an amount not to exceed the following:

''(A) For drugs on the market for at least one year, 10 percent of the annual United States sales revenue during the year prior to which the person is subject to the civil penalty, based upon data from IMS Health Inc.'s Retail and Provider Prospective

Combined Purchases on the United States sales revenue of the drug or, in the event IMS data is not available, based upon any comparable data.

''(B) For drugs on the market for less than one year, $1,000,000.''.

(C) in paragraph (2)(C)), by striking ''paragraph (3)(A)'' and inserting ''paragraph (4)(A)'';

(D) in paragraph (4), as so redesignated, by striking ''paragraph (1) or (2)'' each place it appears and inserting ''paragraph (1), (2), or (3)''; and

(E) in paragraph (6), as so redesignated, by striking ''paragraph (4)'' each place it appears and inserting ''paragraph (5)''.

SEC. 3. NO EFFECT ON WITHDRAWAL OR SUSPENSION OF APPROVAL.

Section 505(e) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(e)) is amended by adding at the end the following: ''The Secretary may withdraw the approval of an application submitted under this section, or suspend the approval of such an application, as provided under this subsection, without first ordering the applicant to submit an assessment of the approved risk eval-

uation and mitigation strategy for the drug under section 505A(g)(2)(E).''.

SEC. 4. BENEFIT-RISK ASSESSMENTS.

Not later than 1 year after the date of the enactment of this Act, the Commissioner of Food and Drugs shall submit to the Congress a report on how best to communicate to the public the risks and benefits of new drugs and the role of the risk evaluation and mitigation strategy in assessing such risks and benefits.

SEC. 5. ROUTINE ACTIVE SURVEILLANCE AND ASSESSMENT.

(a) IN GENERAL.—Subsection (k) of section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) is amended by adding at the end the following:

''(3) ROUTINE ACTIVE SURVEILLANCE AND ASSESSMENT.—

''(A) DEVELOPMENT OF THE POSTMARKET RISK IDENTIFICATION AND ANALYSIS SYSTEM.—The Secretary shall, not later than 2 years after the date of enactment of the Enhancing Drug Safety and Innovation Act of 2007, act in collaboration with academic institutions and private entities to—

''(I) establish minimum standards for collection and transmission of post-

marketing data elements from electronic health data systems; and

''(ii) establish, through partnerships, a validated and integrated postmarket risk identification and analysis system to integrate and analyze safety data from multiple sources, with the goals of including, in aggregate—

''(I) at least 25,000,000 patients by July 1, 2010; and

''(II) at least 100,000,000 patients by July 1, 2012.

''(B) DATA COLLECTION ACTIVITIES.—

''(I) IN GENERAL.—The Secretary shall, not later than 1 year after the establishment of the minimum standards and the identification and analysis system under subparagraph (A), establish and maintain an active surveillance infrastructure—

''(I) to collect and report data for pharmaceutical postmarket risk identification and analysis, in compliance with the regulations promulgated under section 264(c)) of the Health

Insurance Portability and Accountability Act of 1996; and

"(II) that includes, in addition to the collection and monitoring (in a standardized form) of data on all serious adverse drug experiences (as defined in section 505A(b)) required to be submitted to the Secretary under paragraph (1), and those events voluntarily submitted from patients, providers, and drug, when appropriate, procedures to—

"(aa) provide for adverse event surveillance by collecting and monitoring Federal health-related electronic data (such as data from the Medicare program and the health systems of the Department of Veterans Affairs);

"(bb) provide for adverse event surveillance by collecting and monitoring private sector health-related electronic data (such as pharmaceutical purchase

data and health insurance claims data);

''(cc) provide for adverse event surveillance by monitoring standardized electronic health records, as available;

''(dd) provide for adverse event surveillance by collecting and monitoring other information as the Secretary deems necessary to create a robust system to identify adverse events and potential drug safety signals;

''(ee) enable the program to identify certain trends and patterns with respect to data reported to the program;

''(ff) enable the program to provide regular reports to the Secretary concerning adverse event trends, adverse event patterns, incidence and prevalence of adverse events, laboratory data, and other information determined appropriate, which may include

data on comparative national adverse event trends; and

''(gg) enable the program to export data in a form appropriate for further aggregation, statistical analysis, and reporting.

''(ii) TIMELINESS OF REPORTING.—The procedures developed under clause (I) shall ensure that such data are collected, monitored, and reported in a timely, routine, and automatic manner, taking into consideration the need for data completeness, coding, cleansing, and transmission.

''(iii) PRIVATE SECTOR RESOURCES.—To ensure the establishment of the active surveillance infrastructure by the date described under clause (I), the Secretary may, on a temporary or permanent basis, implement systems or products developed by private entities.

''(iv) COMPLEMENTARY APPROACHES.—To the extent the active surveillance infrastructure established under clause (I) is not sufficient to gather data and information relevant to priority drug

safety questions, the Secretary shall develop, support, and participate in complementary approaches to gather and analyze such data and information, including—

"(I) approaches that are complementary with respect to assessing the safety of use of a drug in domestic populations not included in the trials used to approve the drug (such as older people, people with comorbidities, pregnant women, or children); and

"(II) existing approaches such as the Vaccine Adverse Event Reporting System and the Vaccine Safety Datalink or successor databases.

"(v) AUTHORITY FOR CONTRACTS.—The Secretary may enter into contracts with public and private entities to fulfill the requirements of this subparagraph.

"(C) RISK IDENTIFICATION AND ANALYSIS.—

"(I) PURPOSE.—To carry out this paragraph, the Secretary shall establish

collaborations with other Government, academic, and private entities, including the Centers for Education and Research on Therapeutics under section 912 of the Public Health Service Act, to provide for the risk identification and analysis of the data collected under subparagraph (B) and data that is publicly available or is provided by the Secretary, in order to—

"(I) improve the quality and efficiency of postmarket drug safety risk-benefit analysis;

"(II) provide the Secretary with routine access to expertise to study advanced drug safety data; and

"(III) enhance the ability of the Secretary to make timely assessments based on drug safety data.

"(ii) PUBLIC PROCESS FOR PRIORITY QUESTIONS.—At least biannually, the Secretary shall seek recommendations from the Drug Safety and Risk Management Advisory Committee (or successor committee) and from other advisory commit-

tees, as appropriate, to the Food and Drug Administration on—

"(I) priority drug safety questions; and

"(II) mechanisms for answering such questions, including through—

"(aa) routine active surveillance under subparagraph (B); and

"(bb) when such surveillance is not sufficient, postmarket studies under paragraph (4) of section 505A(e) and postapproval clinical trials under paragraph (5) of such section.

"(iii) PROCEDURES FOR THE DEVELOPMENT OF DRUG SAFETY COLLABORATIONS.—

"(I) IN GENERAL.—Not later than 180 days after the date of the establishment of the active surveillance infrastructure under subparagraph (B), the Secretary shall establish and implement procedures under

which the Secretary may routinely collaborate with a qualified entity to—

"(aa) clean, classify, or aggregate data collected under subparagraph (B) and data that is publicly available or is provided by the Secretary;

"(bb) allow for prompt investigation of priority drug safety questions, including—

"(AA) unresolved safety questions for drugs or classes of drugs; and

"(BB) for a newly-approved drug: safety signals from clinical trials used to approve the drug and other preapproval trials; rare, serious drug side effects; and the safety of use in domestic populations not included in the trials used to approve the drug (such as older people, people with

comorbidities, pregnant women, or children);

''(cc) perform advanced research and analysis on identified drug safety risks;

''(dd) convene an expert advisory committee to oversee the establishment of standards for the ethical and scientific uses for, and communication of, postmarketing data collected under subparagraph (B), including advising on the development of effective research methods for the study of drug safety questions;

''(ee) focus postmarket studies under paragraph (4) of section 505A(e) and postapproval clinical trials under paragraph (5) of such section more effectively on cases for which reports under paragraph (1) and other safety signal detection is not sufficient to resolve whether there is an elevated risk of a serious ad-

verse event associated with the use of a drug; and

''(ff) carry out other activities as the Secretary deems necessary to carry out the purposes of this paragraph.

''(II) REQUEST FOR SPECIFIC METHODOLOGY.—The procedures described in subclause (I) shall permit the Secretary to request that a specific methodology be used by the qualified entity. The qualified entity shall work with the Secretary to finalize the methodology to be used.

''(iv) USE OF ANALYSES.—The Secretary shall provide the analyses described under this subparagraph, including the methods and results of such analyses, about a drug to the sponsor or sponsors of such drug.

''(v) QUALIFIED ENTITIES.—

''(I) IN GENERAL.—The Secretary shall enter into contracts with a sufficient number of qualified entities to develop and provide informa-

tion to the Secretary in a timely manner.

''(II) QUALIFICATION.—The Secretary shall enter into a contract with an entity under subclause (I) only if the Secretary determines that the entity—

''(aa) has the research capability and expertise to conduct and complete the activities under this paragraph;

''(bb) has in place an information technology infrastructure to support adverse event surveillance data and operational standards to provide security for such data;

''(cc) has experience with, and expertise on, the development of drug safety and effectiveness research using electronic population data;

''(dd) has an understanding of drug development and risk/

benefit balancing in a clinical setting; and

"(ee) has a significant business presence in the United States.

"(vi) CONTRACT REQUIREMENTS.—Each contract with a qualified entity shall contain the following requirements:

"(I) ENSURING PRIVACY.—The qualified entity shall provide assurances that the entity will not use the data provided by the Secretary in a manner that violates—

"(aa) the regulations promulgated under section 264(c)) of the Health Insurance Portability and Accountability Act of 1996; or

"(bb) sections 552 or 552a of title 5, United States Code, with regard to the privacy of individually-identifiable beneficiary health information.

"(II) COMPONENT OF ANOTHER ORGANIZATION.—If a qualified entity

is a component of another organization—

"(aa) the qualified entity shall maintain the data related to the activities carried out under this paragraph separate from the other components of the organization and establish appropriate security measures to maintain the confidentiality and privacy of such data; and

"(bb) the entity shall not make an unauthorized disclosure of such data to the other components of the organization in breach of such confidentiality and privacy requirement.

"(III) TERMINATION OR NONRENEWAL.—If a contract with a qualified entity under this subparagraph is terminated or not renewed, the following requirements shall apply:

"(aa) CONFIDENTIALITY AND PRIVACY PROTECTIONS.—The entity shall continue to com-

ply with the confidentiality and privacy requirements under this paragraph with respect to all data disclosed to the entity.

''(bb) DISPOSITION OF DATA.—The entity shall return to the Secretary all data disclosed to the entity or, if returning the data is not practicable, destroy the data.

''(vii) COMPETITIVE PROCEDURES.—The Secretary shall use competitive procedures (as defined in section 4(5) of the Federal Procurement Policy Act) to enter into contracts under clause (v).

''(viii) REVIEW OF CONTRACT IN THE EVEN OF A MERGER OR ACQUISITION.—The Secretary shall review the contract with a qualified entity under this paragraph in the event of a merger or acquisition of the entity in order to ensure that the requirements under this subparagraph will continue to be met.

''(D) COORDINATION.—In carrying out this paragraph, the Secretary shall provide for

appropriate communications to the public, scientific, public health, and medical communities, and other key stakeholders, and provide for the coordination of the activities of private entities, professional associations, or other entities that may have sources of surveillance data.''.

(b) AUTHORIZATION OF APPROPRIATIONS.—To carry out activities under the amendment made by subsection (a) for which funds are made available under section 736 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 379h), there are authorized to be appropriated to carry out the amendment made by this section, in addition to such funds, $25,000,000 for each of fiscal years 2008 through 2012.

SEC. 6. RULE OF CONSTRUCTION REGARDING FEDERAL PREEMPTION.

Nothing in this Act or the amendments made by this Act may be construed as having any legal effect on any cause of action for damages under the law of any State (including statutes, regulations, and common law).

SEC. 7. AUTHORIZATION OF APPROPRIATIONS.

(a) IN GENERAL.—For carrying out this Act and the amendments made by this Act, there is authorized to be appropriated $25,000,000 for each of fiscal years 2008 through 2012.

(b) RELATION TO OTHER FUNDING.—The authorization of appropriations under subsection (a) is in addition to any other funds available for carrying out this Act and the amendments made by this Act.

SEC. 8. EFFECTIVE DATE AND APPLICABILITY.

(a) EFFECTIVE DATE.—This Act takes effect 180 days after the date of the enactment of this Act.

(b) DRUGS DEEMED TO HAVE RISK EVALUATION AND MITIGATION STRATEGIES.—

(1) IN GENERAL.—A drug that was approved before the effective date of this Act is, in accordance with paragraph (2), deemed to have in effect an approved risk evaluation and mitigation strategy under section 505A of the Federal Food, Drug, and Cosmetic Act (as added by section 1 of this Act) (referred to in this section as the ''Act'') if there are in effect on the effective date of this Act restrictions on distribution or use—

(A) required under section 314.520 or section 601.42 of title 21, Code of Federal Regulations; or

(B) otherwise agreed to by the applicant and the Secretary for such drug.

(2) ELEMENTS OF STRATEGY; ENFORCEMENT.—The approved risk evaluation and mitigation strategy in effect for a drug under paragraph (1)—

(A) is deemed to consist of the elements described in paragraphs (1) and (2) of section 505A(d) of the Act and any additional elements under subsections (d) and (e) of such section in effect for such drug on the effective date of this Act; and

(B) is subject to enforcement by the Secretary to the same extent as any other risk evaluation and mitigation strategy under section 505A of the Act.

(3) SUBMISSION.—Not later than 180 days after the effective date of this Act, the holder of an approved application for which a risk evaluation and mitigation strategy is deemed to be in effect under paragraph (1) shall submit to the Secretary a proposed risk evaluation and mitigation strategy. Such proposed strategy is subject to section 505A of the Act as if included in such application at the time of submission of the application to the Secretary.

(c) OTHER DRUGS APPROVED BEFORE THE EFFECTIVE DATE.—The Secretary, on a case-by-case basis, may require the holder of an application approved before the

effective date of this Act to which subsection (b) does not apply to submit a proposed risk evaluation and mitigation strategy in accordance with the timeframes provided for in subparagraphs (C) through (E) of section 505A(g)(2) of the Act if the Secretary determines (with respect to such drug or with respect to the group of drugs to which such drug belongs) that—

(1) an element described under 505A(d)(1) of the Act may require modification; or

(2) a standard for adding an element described in subsection (e) or (d) of the Act that is not in effect with respect to such drug or class of drugs may apply.

(d) USE OF ADVISORY COMMITTEES; PROCESS FOR ADDRESSING DRUG CLASS EFFECTS.—In imposing a requirement under subsection (c), the Secretary—

(1) may convene a meeting of 1 or more advisory committees of the Food and Drug Administration in accordance with paragraph (6) of section 505A(h) of the Act; and

(2) may use the process described in paragraph (7) of such section 505A(h) (relating to addressing drug class effects).